09/818,066

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	2489	530/324.ccls.	USPAT; US-PGPUB	2002/05/11 14:40			0
2	BRS	L3	691	530/325.ccls.	USPAT; US-PGPUB	2002/05/11 14:42			0
3	BRS	L4	1513	530/326.ccls.	USPAT; US-PGPUB	2002/05/11 14:40			0
4	BRS	L5	6655	530/350.ccls.	USPAT; US-PGPUB	2002/05/11 14:40			0
5	BRS	L6	229	530/826.ccls.	USPAT; US-PGPUB	2002/05/11 14:41			0
6	BRS	L7	7522	435/69.1.ccls.	USPAT; US-PGPUB	2002/05/11 14:41			0
7	BRS	L8	1332	435/69.7.ccls.	USPAT; US-PGPUB	2002/05/11 14:41			0
8	BRS	L9	15087	1 or 3 or 4 or 5 or 6 or 7 or 8	USPAT; US-PGPUB	2002/05/11 14:42			0
9	BRS	L10	3608	hepatitis adj b adj virus	USPAT; US-PGPUB	2002/05/11 14:42			0
10	BRS	L11	289	hepadnavirus	USPAT; US-PGPUB	2002/05/11 14:42			0
11	BRS	L12	3722	10 or 11	USPAT; US-PGPUB	2002/05/11 14:42			0
12	BRS	L13	244	pre adj s	USPAT; US-PGPUB	2002/05/11 14:42			0
13	BRS	L14	73	9 and 12 and 13	USPAT; US-PGPUB	2002/05/11 14:43			0

09/818,066

Set	Items	Description
S1	2616	HEPADNAVIRUS
S2	119908	HEPATITIS(W)B(W)VIRUS
S3	120677	S1 OR S2
S4	372	PRE(W)S(W)PROTEIN
S5	9474	RECEPTOR(W)BINDING(W)SITE
S6	9826	S4 OR S5
S7	372	S3(S)S6
S8	90301	GLUTATHIONE(W)S(W)TRANSFERASE
S9	25	S7 AND S8
S10	9	S9 NOT PY>1995
S11	5	RD (unique items)
S12	199	S7 NOT PY>1995
S13	91	RD (unique items)
S14	87	S13 NOT S11
S15	439	AU='TONG S'
S16	204	AU='TONG S.'
S17	31	AU='TONG SHUPING'
S18	26	AU='LI JISU'
S19	1964	AU='WANDS J' OR AU='WANDS J R' OR AU='WANDS J.' OR AU='WANDS J.R.' OR AU='WANDS JACK' OR AU='WANDS JACK R' OR AU='WANDS JACKS R' OR AU='WANDS JAKC R' OR AU='WANDS JR'
S20	2591	S15 OR S16 OR S17 OR S18 OR S19
S21	28	S20 AND S3 AND S6
S22	4	S21 NOT PY>1995
S23	2	RD (unique items)

?

09/818,066

Set	Items	Description
S1	1	SEPHADEX
S2	250	TRITON
S3	0	TRITON(W)X
S4	2	GIGAPACK

09/818,066

Set	Items	Description
S1	16905	HEPATITIS(W)B(W)VIRUS
S2	336	ESCAPE(W)MUTANT? ?
S3	65	S1 AND S2
S4	65	RD (unique items)

?

11/3,AB/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09997467 BIOSIS NO.: 199598452385
Efficient expression, purification and characterization of hepatitis B virus PRES1 protein from Escherichia coli.
AUTHOR: Kim Hee Sun; Hong Hyo Jeong(a)
AUTHOR ADDRESS: (a)Protein Eng. Res. Group, Korea Res. Inst. Biosci. Biotechnol., KIST, P.O. Box 115, Yuseong, Taej**South Korea

JOURNAL: Biotechnology Letters 17 (8):p871-876 1995
ISSN: 0141-5492
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The complete (encoding 119 aminon acids, aa) or partial (encoding the N-terminal 90 aa) preS1 region gene of **hepatitis B virus** (HBV) was fused to the 3'-end of **glutathione - S - transferase** (GST) gene and expressed at 37 degree C under the control of the inducible tac promoter in E. coli. The results showed that the fusion protein with the full length of preS1 was moderately expressed, about 10% of total cellular proteins, while the protein with the partial preS1 was highly expressed, about 33% of total cellular proteins but the half was degraded into the protein with about N-terminal 60 aa of preS1. Accordingly, GST fusion protein containing the N-terminal 56 aa of the preS1, which still encodes B-and T-cell epitopes and a hepatocyte **receptor binding site** , was expressed under the same induction conditions and was shown to be highly and stably expressed, about 37% of total cellular proteins. The fusion protein with the full length or N-terminal 56 aa of preS1 and the peptides were simply and successfully purified by affinity chromatography and were demonstrated to exhibit the antigenicity and immunogenicity of the preS1 antigen.

1995

11/3,AB/2 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01096704 Genuine Article#: FW027 Number of References: 13
Title: INHIBITORY ACTIVITY OF MONOCLONAL ANTIBODY-F35.25 ON THE INTERACTION BETWEEN HEPATOCYTES (HEPG2-CELLS) AND PRES1-SPECIFIC LIGANDS (Abstract Available)
Author(s): PETIT MA; STRICK N; DUBANCHET S; CAPEL F; NEURATH AR
Corporate Source: INSERM,U131,UNITE IMMUNOPATHOL & IMMUNOL VIRALE,32 RUE CARNETS/F-92140 CLAMART//FRANCE/; NEW YORK BLOOD CTR,LINDSLEY F KIMBALL RES INST/NEW YORK//NY/10021
Journal: MOLECULAR IMMUNOLOGY, 1991, V28, N4-5, P517-521
Language: ENGLISH Document Type: ARTICLE
Abstract: The capacity of a preS1-specific monoclonal antibody (McAb) F35.25 to block the attachment of preS1-specific ligands to human hepatoma HepG2 cells was studied. In order to define more precisely the fine epitope specificity of McAb F35.25, its reaction with synthetic peptides derived from the preS1 sequence (12-53) was investigated. McAb F35.25 was found to recognize better synthetic peptide preS(21-47) from the adw 2 and ayw sequences than the synthetic peptide preS(32-53) adw 2. The shortest sequence recognized by McAb F35.25 among the peptide sequences studied was preS(32-47). The corresponding amino acid sequence (for HBV subtype adw 2) is PAFGANSNNPDWDFNP. As expected, it was found that McAb F35.25 inhibited the attachment of HepG2 cells to HBsAg-cellulose, as well as to preS(21-47)-cellulose, corresponding to two HBV subtypes adw 2 and ayw. Finally, the inhibitory effect of different peptides on the interaction

of McAb F35.25 with HBsAg particles containing the preS1 sequence was also studied. The peptide preS(12-47) appeared to be the most effective inhibitor. Therefore, the McAb F35.25 is specific for the sequence preS1(X to 47), where (12 less-than-or-equal-to X < 32). These results indicate that McAb F35.25 is probably virus-neutralizing and represents a reagent of great value to study the interaction between HBV and hepatocytes independently of d/y subtype changes.

11/3,AB/3 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

00114115 Genuine Article#: CN825 Number of References: 69
Title: VIRUS-NEUTRALIZING MONOCLONAL-ANTIBODY TO A CONSERVED EPITOPE ON THE DUCK HEPATITIS B - VIRUS PRE - S PROTEIN
Author(s): LAMBERT V; FERNHOLZ D; SPRENGEL R; FOUREL I; DELEAGE G; WILDNER G; PEYRET C; TREPO C; COVA L; WILL H
Corporate Source: CNRS,PHYSICOCHIM BIOL LBTM LAB,UMR9/F-69622 VILLEURBANNE//FRANCE/; CNRS,PHYSICOCHIM BIOL LBTM LAB,UMR9/F-69622 VILLEURBANNE//FRANCE/; INSERM,U271,RECH HEPATITES LAB/F-69003 LYONS//FRANCE/; MAX PLANCK INST BIOCHEM/D-8033 MARTINSRIED//FEDREP GER/
Journal: JOURNAL OF VIROLOGY, 1990, V64, N3, P1290-1297
Language: ENGLISH Document Type: ARTICLE

11/3,AB/4 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

12258394 PASCAL No.: 95-0484063
Efficient expression, purification and characterization of hepatitis B virus preS1 protein from Escherichia coli
HEE SUN KIM; HYO JEONG HONG
KIST, Korea res. inst. biosci. biotechnology, protein eng. res. group, Taejon 305-600, Republic of Korea
Journal: Biotechnology letters, 1995, 17 (8) 871-876
Language: English
The complete (encoding 119 amino acids, aa) or partial (encoding the N-terminal 90 aa) preS1 region gene of **hepatitis B virus** (HBV) was fused to the 3'-end of **glutathione - S - transferase** (GST) gene and expressed at 37 Degree C under the control of the inducible tac promoter in E. coli. The results showed that the fusion protein with the full length of preS1 was moderately expressed, about 10% of total cellular proteins, while the protein with the partial preS1 was highly expressed, about 33% of total cellular proteins but the half was degraded into the protein with about N-terminal 60 aa of preS1. Accordingly, GST fusion protein containing the N-terminal 56 aa of the preS1, which still encodes B-and T-cell epitopes and a hepatocyte **receptor binding site** , was expressed under the same induction conditions and was shown to be highly and stably expressed, about 37% of total cellular proteins. The fusion protein with the full length or N-terminal 56 aa of preS1 and the peptides were simply and successfully purified by affinity chromatography and were demonstrated to exhibit the antigenicity and immunogenicity of the preS1 antigen.

11/3,AB/5 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

122283391 CA: 122(23)283391b JOURNAL
Expression in E. coli of the chimeric genes in which the PreS coding region of the surface antigen of hepatitis B virus was fused to a glutathione S-transferase gene
AUTHOR(S): Liu, Hui; Li, Zaiping; Yu, Xianming
LOCATION: Shanghai Inst. Biochem., Academia Sinica, Peop. Rep. China,

200131
JOURNAL: Shengwu Huaxue Yu Shengwu Wuli Xuebao DATE: 1994 VOLUME: 26
NUMBER: 5 PAGES: 513-18 CODEN: SHWPAU ISSN: 0582-9879 LANGUAGE:
Chinese
?

14/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08673531 96105350 PMID: 7503692
Expression and characterization of the multiplied, recombinant preS1 antigen of hepatitis B virus.
Sidorkiewicz M; Pluciennicz G; Pluciennicz A
Department of Biochemistry, Medical University of Lodz, Poland.
Archives of virology (AUSTRIA) 1995, 140 (11) p1935-44, ISSN 0304-8608 Journal Code: 8L7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The amino acid sequence encoded by the preS1 region of **hepatitis B virus** genome is expressed on the surface of virions and subviral particles. The preS1 region is involved in the recognition of specific receptors responsible for the attachment of HBV to the host cell. The cell **receptor binding site** was assigned to the preS1 (20-47 aa) fragment. In order to obtain a large quantity of preS1 binding domains of HBV the expression vector pWX4 was constructed. It contains four tandemly joined DNA sequences, each coding for preS1 (20-49 aa), fused with the 3' end of a DNA fragment coding for 450 aa of beta-galactosidase. E. coli cells transformed with this vector produce fusion protein beta-gal-preS1x4 in the form of inclusion bodies. Owing to the specific trypsin digestion, the preS1x4 domain was cleaved from the fusion protein. The resulting product, a 16 kDa protein, was isolated and purified by anion exchange chromatography. The presence of four Asp-Pro bonds in this sequence and the primary structure of the first 28 N-terminal amino acids were determined. Following the confirmation of the antigenic properties, the recombinant preS1 protein was used for detection of the anti-preS1 response in sera from HBV infected patients.

14/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08391484 94368485 PMID: 7765264
High level expression of hepatitis B virus preS1 peptide in Escherichia coli.
Rhyum SB; Jin BR; Park HR; Hong HJ
Protein Engineering Research Group, Genetic Engineering Research Institute, KIST, Taejon, South Korea.
Journal of biotechnology (NETHERLANDS) Aug 31 1994, 36 (3) p221-30, ISSN 0168-1656 Journal Code: AL6
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
PreS1 region gene fragment encoding the N-terminal 56 amino acid (aa) of **hepatitis B virus** (HBV, adr subtype), which encodes B- and T-cell epitopes and an hepatocyte **receptor binding site** , was synthesized by PCR and fused to the 3'-end of MalE gene encoding maltose-binding protein (MBP) to yield expression plasmid pMalpreS1-56. The plasmid was introduced into Escherichia coli DH5 alpha and expressed at 37 degrees C under the control of inducible tac promoter. The resulting fusion protein was highly expressed in a soluble form, about 40% of total cellular proteins, but it bound only partially to an amylose column. Therefore, the soluble preS1 fusion protein was purified to near homogeneity by two passages of anion-exchange chromatography followed by gel filtration. The yield of the fusion protein was 70 mg per 1 culture that had been induced by IPTG for 6 h. The purified fusion protein was specifically cleaved by a Factor Xa digestion to release the preS1 peptide, which was then purified by gel filtration to homogeneity. The purity, integrity, antigenicity and immunogenicity of the purified preS1 peptide was confirmed by glycerol-SDS-PAGE, Western analysis, N-terminal amino acid sequencing and an indirect ELISA.

14/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08383884 95088618 PMID: 7527840
A modified hepatitis B virus **surface antigen with the** receptor - binding site **for hepatocytes at its C terminus: expression, antigenicity and immunogenicity.**
Xu X; Li GD; Kong YY; Yang HL; Zhang Z; Cao HT; Wang Y
Shanghai Institute of Biochemistry, Academia Sinica, People's Republic of China.
Journal of general virology (ENGLAND) Dec 1994, 75 (Pt 12) p3673-7, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A modified **hepatitis B virus** (HBV) surface antigen, the SA-28 protein, was constructed and expressed by recombinant vaccinia virus in mammalian cells. This protein was composed of a PreS1 region-derived peptide (amino acids 21 to 47) that contained the hepatocyte **receptor - binding site** , joined to the C terminus of the major S protein at amino acid position 223. This modified surface antigen could be efficiently assembled into particles with a density of 1.23 g/ml and could be secreted from several mammalian cell lines. The results of immunoprecipitation revealed that the SA-28 protein was recognized by both the anti-S protein antibody and the anti-PreS1 antibody. A strong antibody response, against both the S protein and PreS1 epitopes, was induced in BALB/c mice immunized by the SA-28 particles indicating good immunogenicity. These results suggested that the HBV surface antigen consisting of the SA-28 protein could be a promising candidate as a new HBV vaccine with higher efficacy.

14/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08374954 94174740 PMID: 7510440
Identification of major antigenic domains of duck hepatitis B virus pre - S protein **by peptide scanning.**
Chassot S; Lambert V; Kay A; Godinot C; Trepo C; Cova L
INSERM U 271, Lyon, France.
Virology (UNITED STATES) Apr 1994, 200 (1) p72-8, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Neutralization epitopes of duck **hepatitis B virus** (DHBV) have been previously mapped within the N-terminal portion of the **pre - S protein** using monoclonal antibodies. However, the immune response of ducks to this region is not well characterized at the amino acid level. To this end, we have immunized adult Pekin ducks with either DHBV positive serum or bacterially expressed DHBpre-S polypeptide representing the N-terminal portion of the DHBV pre-S region. We have demonstrated that adult ducks inoculated with either antigen developed antibodies to the DHBV pre-S region starting 5 to 10 days postinjection. The sera of all ducks, irrespective of the immunogen used, exhibited a significant protective activity against DHBV, as assessed in vivo. To identify which pre-S domains bind antibodies from these duck sera, we have used the Pepscan methodology with overlapping octapeptides spanning the DHBV pre-S sequence from amino acids 1 to 145. Using this approach, five major antigenic domains, 7KSMDVRRI14, 22NQLAGRMIP30, 58TLQNQGAW65, 71RRVGLSNPT79, and 127GDDPLLGNQ135 were identified within the DHBV pre-S region.

14/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07552263 92024107 PMID: 1718087

In vivo neutralization of duck hepatitis B virus **by antibodies specific to the N-terminal portion of** pre - S protein .

Lambert V; Chassot S; Kay A; Trepo C; Cova L

INSERM U 271, Lyon, France.

Virology (UNITED STATES) Nov 1991, 185 (1) p446-50, ISSN 0042-6822 Journal Code: XEA

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

The neutralization of duck hepatitis B virus (DHBV) infection using antibodies directed against the N-terminal portion of the large surface protein was examined in vitro and in vivo. We demonstrate here that a monoclonal antibody, directed against an epitope mapped between aa 77 and aa 100 on the DHBV pre-S, exerts a similar neutralizing activity (77%) both in vivo and in vitro. Furthermore, we have found that a polyclonal antiserum raised against the bacterially expressed 131 first amino acids of the DHBV pre-S region abolished the infectivity of DHBV in ducklings. Therefore, antibodies against a peptide representing most of the DHBV pre-S region (1-131) or a monoclonal antibody specific to an epitope within this region neutralizes in vivo DHBV infectivity.

14/3,AB/14 (Item 14 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07159272 93371677 PMID: 8363732

The properties of an HBV surface antigen protein carrying the binding site for the receptor of hepatocytes--its formation of surface antigen particles and secretion from discrete cell lines.

Yu XM; Li ZP

Shanghai Institute of Biochemistry, Academia Sinica, PRC.

Science in China. Series B, Chemistry, life sciences & earth sciences (CHINA) Jun 1993, 36 (6) p685-92, ISSN 1001-652X Journal Code: AEU

Contract/Grant No.: CA-07175, CA, NCI; CA-22443, CA, NCI

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

A human **hepatitis B virus** (HBV) gene, which encodes the major surface antigen protein (S protein) carrying the hepatocyte **receptor - binding site** , was constructed with site-directed mutagenesis and in vitro recombination. When expressed in monkey kidney cell line COS-M6, this gene product (S309 protein) formed surface antigen (HBsAg) particles and secreted from the cells. It was stable within the cells and in the culture medium and could be immunoprecipitated with antisera directed against plasma-derived HBsAg or synthetic preS1 polypeptide. Isopycnic CsCl gradient centrifugation showed that the density of S309 protein particles (1.25 g/ml) was slightly higher than that of S protein particles. The S309 protein was readily secretable from hepatoma cell lines, and the amount secreted was comparable to that of the S protein. By contrast, only about 10% of the S309 protein was secreted from COS-M6 cells, and its appearance in culture medium was delayed. The efficiency of the secretion of the S309 protein can be improved when it is coexpressed with the S protein.

14/3,AB/15 (Item 15 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07139043 93297108 PMID: 7685963

Fine mapping of neutralization epitopes on duck hepatitis B virus **(DHBV)** pre - S protein **using monoclonal antibodies and overlapping peptides.**

Chassot S; Lambert V; Kay A; Godinot C; Roux B; Trepo C; Cova L

INSERM U 271, Lyon, France.

Virology (UNITED STATES) Jan 1993, 192 (1) p217-23, ISSN 0042-6822

Journal Code: XEA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

To define the residues involved in duck **hepatitis B virus** (DHBV) neutralization at the amino acid level, we have used a procedure combining monoclonal antibodies (MAbs) and overlapping octapeptides (Pepscan). Two neutralizing MAbs (SD20 and 900), specific for the **pre - S protein** were shown to reduce DHBV infectivity in vivo by 75 and 90%, respectively, while complete protection of ducklings was achieved with a polyclonal antiserum raised against the bacterially expressed first 131 amino acids of the DHBV pre-S region (DHBpre-S). Using fusion polypeptides, the binding sites of these MAbs were localized between aa 77 and 100 on **pre - S protein**. We have used octapeptides spanning the pre-S sequence from aa 64 to 115 for fine mapping of these epitopes. Within the sequence scanned, the polyclonal anti-DHBpre-S antiserum recognized a region exclusively limited to the residues E82-K95, suggesting immunodominance of this region in the sequence aa 64-115. The epitope recognized by Mab 900 was mapped within the same region, whereas the epitope recognized by Mab SD20 was localized downstream from this region. To define the amino acids essential for binding to the highly neutralizing Mab 900, we have used single amino acid replacement and demonstrated that two residues Q87 and W88 were important for antibody recognition.

14/3,AB/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06831458 90156529 PMID: 1689393

Virus-neutralizing monoclonal antibody to a conserved epitope on the duck hepatitis B virus pre - S protein .

Lambert V; Fernholz D; Sprengel R; Fourel I; Deleage G; Wildner G; Peyret C; Trepo C; Cova L; Will H

Laboratoire de Recherche sur le hepatites, Institut National de la Sante et de la Recherche Medicale U 271, Lyon, France.

Journal of virology (UNITED STATES) Mar 1990, 64 (3) p1290-7, ISSN 0022-538X Journal Code: KCV

Languages: ENGLISH
Document type: Journal Article
Record type: Completed

In this study we used duck **hepatitis B virus** (DHBV)-infected Pekin ducks and heron **hepatitis B virus** (HHBV)-infected heron tissue to search for epitopes responsible for virus neutralization on pre-S proteins. Monoclonal antibodies were produced by immunizing mice with purified DHBV particles. Of 10 anti-DHBV specific hybridomas obtained, 1 was selected for this study. This monoclonal antibody recognized in both DHBV-infected livers and viremic sera a major (36-kilodalton) protein and several minor pre-S proteins in all seven virus strains used. In contrast, pre-S proteins of HHBV-infected tissue or viremic sera did not react. Thus, the monoclonal antibody recognizes a highly conserved DHBV pre-S epitope. For mapping of the epitope, polypeptides from different regions of the DHBV pre-S/S gene were expressed in Escherichia coli and used as the substrate for immunoblotting. The epitope was delimited to a sequence of approximately 23 amino acids within the pre-S region, which is highly conserved in four cloned DHBV isolates and coincides with the main antigenic domain as predicted by computer algorithms. In in vitro neutralization assays performed with primary duck hepatocyte cultures, the antibody reduced DHBV infectivity by approximately 75%. These data demonstrate a conserved epitope of the DHBV **pre - S protein** which is located on the surface of the viral envelope and is recognized by virus-neutralizing antibodies.

14/3,AB/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06671711 91037982 PMID: 2230741

A synthetic peptide elicits antibody reactive with the native duck hepatitis B virus pre - S protein .
Wen YM; Xu YY; Zhang W; Liu YZ
Department of Microbiology, Shanghai Medical University, People's Republic of China.
Journal of general virology (ENGLAND) Oct 1990, 71 (Pt 10) p2467-9, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Synthetic peptides P37-49 and P63-79, derived from the pre-S region of duck hepatitis B virus (DHBV), have been synthesized. Only P37-49 was reactive with rabbit anti-DHBs/pre-S antibodies by radioimmunoprecipitation . Antiserum prepared against P37-47 reacted with a 35K polypeptide of native DHBs/pre-S by immunoblotting. It is concluded that P37-49 (MGQHPAKSMDVRR) mimics one of the epitopes of the DHBV pre-S antigen.

14/3,AB/21 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05747817 86272090 PMID: 3015414
Identification and chemical synthesis of a host cell receptor binding site **on** hepatitis B virus .
Neurath AR; Kent SB; Strick N; Parker K
Cell (UNITED STATES) Aug 1 1986, 46 (3) p429-36, ISSN 0092-8674 Journal Code: CQ4
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Hepatitis B virus (HBV) has not yet been propagated in vitro, and knowledge concerning its reaction with receptors on target cells remained scant. We have located within the HBV envelope proteins a sequence mediating the attachment of HBV to human hepatoma HepG2 cells. A synthetic peptide analog (PLGFFPDHQLDPAFGANSNNPDWDFNP) is recognized by both cell receptors and anti-HBV antibodies and elicits antibodies reacting with native HBV. The synthetic peptide is a promising immunogen expected to elicit protective antibodies based on the concept of the attachment blockade pathway of virus neutralization. The approach described here, based on anti-peptide antisera and the binding of peptide analogs to cell receptors is generally applicable for the delineation of cell receptor binding sites on viruses with known gene sequences.

14/3,AB/22 (Item 22 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05578511 89364847 PMID: 2475766
A monoclonal antibody specific for the hepatocyte receptor binding site **on** hepatitis B virus .
Petit MA; Dubanchet S; Capel F
INSERM Unite 131, Clamart, France.
Molecular immunology (ENGLAND) Jun 1989, 26 (6) p531-7, ISSN 0161-5890 Journal Code: NG1
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The sequence of the preS1 region of the **hepatitis B virus** (HBV) envelope (env) proteins contains a dominant binding site for hepatocytes between residues preS21 and preS47. Purified HBV particles (subtype ad) were used as the immunogen to produce specific monoclonal antibodies (McAbs) against three antigenic regions (S, preS2 and preS1) of the HBV env protein. One McAb, F35.25, was found to be specific for the region 32-53 of the preS1 sequence of HBV, which largely overlapped the hepatocyte **receptor binding site** . The preS1-specific McAb F35.25 reacted with both HBV subtypes, ad and ay, in radioimmunoassays (RIA) and with the large

surface proteins, P39 and GP42, as well as with tryptic fragments preS(1-99/103) and preS(1-113) in Western blotting experiments. This McAb F35.25 preferentially recognized, however, the homologous (ad) preS1 sequence in RIA. The ad/ay amino acid substitution within the hepatocyte **receptor binding site** at position 35 (Gly-Arg) may explain the relative subtype-specificity of F35.25. Finally, the F35.25 epitope was detected in all HBV particles purified from HBeAg-positive human sera, confirming that this preS1 region 32-53 is exposed at the surface of complete virions. Thus, we developed a RIA system allowing us to assess the infectivity of HBV particles by the detection of preS1 sequences associated with the viral hepatocyte receptor. Moreover, it is expected that F35.25 may be a virus-neutralizing antibody by blockage of the attachment of HBV to liver cells.

14/3,AB/24 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10082047 BIOSIS NO.: 199598536965
Interaction between a carboxypeptidase-like protein and neutralizing epitopes of duck hepatitis B virus pre - S protein .
AUTHOR: Tong Shuping; Li Kusu; Wands Jack R
AUTHOR ADDRESS: Molecular Hepatol. Lab., Mass. Gen. Hosp. Cancer Cent., Charlestown, MA 02129**USA
JOURNAL: Hepatology 22 (4 PART 2):p269A 1995
CONFERENCE/MEETING: 46th Annual Meeting and Postgraduate Course of the American Association for the Study of Liver Diseases Chicago, Illinois, USA November 3-7, 1995
ISSN: 0270-9139
RECORD TYPE: Citation
LANGUAGE: English
1995

14/3,AB/37 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

11776096 PASCAL No.: 94-0648157
High level expression of hepatitis B virus preS1 peptide in Escherichia coli
SUN BOON RHYUM; BYUNG RAE JIN; HEUNG ROK PARK; HYO JEONG HONG
KIST, genetic eng. res. inst., protein eng. res. group, Taejon 305-600, Republic of Korea
Journal: Journal of biotechnology, 1994, 36 (3) 221-230
Language: English
PreS1 region gene fragment encoding the N-terminal 56 amino acid (aa) of **hepatitis B virus** (HBM, adr subtype), which encodes B- and T-cell epitopes and an hepatocyte **receptor binding site** , was synthesized by PCR and fused to the 3'-end of Male gene encoding maltosc-binding protein (MBP) to yield expression plasmid pMalpreS1-56. The plasmid was introduced into Escherichia coli DH5 alpha and expressed at 37 SUP o C under the control of inducible tac promoter. The resulting fusion protein was highly expressed in a soluble form, about 40% of total cellular proteins, but it bound only partially to an amylose column. Therefore, the soluble preS1 fusion protein was purified to near homogeneity by two passages of anion-exchange chromatography followed by gel filtration

14/3,AB/38 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal

09369989 PASCAL No.: 91-0160366
A synthetic peptide elicits antibody reactive with the native duck

hepatitis B virus pre- S protein
YU-MEI WEN; YONG-YAO XU; WEI ZHANG; YING-ZHENG LIU
Shanghai medical univ., dep. microbiology, Shanghai 200032, China
Journal: Journal of general virology, 1990, 71 (10) 2467-2469
Language: English
Synthetic peptides P37-49 and P63-79, derived from the pre-S region of duck hepatitis B virus (DHBV), have been synthesized. Only P37-49 was reactive with rabbit anti-DHBs/pre-S antibodies by radioimmunoprecipitation . It is concluded that P37-49 (MGQHPAKSMDVRR) mimics one of the epitopes of the DHBV pre-S antigen

14/3,AB/46 (Item 5 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

122124468 CA: 122(11)124468r JOURNAL
High expression of duck hepatitis B virus pre-S antigen in E. coli and the application of this recombinant protein
AUTHOR(S): Ma, Zhangmei; Li, Boliang; Xiong, Sidong; Wen, Yumei
LOCATION: Laboratory of Molecular Virology, Shanghai Medical University, Shanghai, Peop. Rep. China, 200032
JOURNAL: Bingdu Xuebao DATE: 1994 VOLUME: 10 NUMBER: 1 PAGES: 1-7
CODEN: BIXUEA ISSN: 1000-8721 LANGUAGE: Chinese

14/3,AB/48 (Item 7 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

120188550 CA: 120(15)188550c JOURNAL
Properties of hepatitis B virus pre-S1 deletion mutants
AUTHOR(S): Melegari, Margherita; Bruno, Savino; Wands, Jack R.
LOCATION: Cancer Cent., Massachusetts Gen. Hosp., Boston, MA, 02114, USA
JOURNAL: Virology DATE: 1994 VOLUME: 199 NUMBER: 2 PAGES: 292-300
CODEN: VIRLAX ISSN: 0042-6822 LANGUAGE: English

14/3,AB/49 (Item 8 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

120131539 CA: 120(11)131539b JOURNAL
PreS-sequences of the HBV capsid: molecular biology and immunology
AUTHOR(S): Sominskaya, I. V.; Sergeeva, S. M.; Pumpen, P. P.
LOCATION: Latv. Med. Acad., Latvia,
JOURNAL: Mol. Genet., Mikrobiol. Virusol. DATE: 1993 NUMBER: 3 PAGES: 15-22 CODEN: MGMVDU ISSN: 0208-0613 LANGUAGE: Russian

14/3,AB/52 (Item 11 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

117105342 CA: 117(11)105342a JOURNAL
The expression of duck hepatitis B virus preS antigen in Escherichia coli
AUTHOR(S): Li, Wei; Jiang, Fumei; Zhang, Wei; Wen, Yumei; Zhou, Yongshui; Wu, Xiangfu
LOCATION: Shanghai Inst. Biochem., Acad. Sin., Shanghai, Peop. Rep. China, 200031
JOURNAL: Shengwu Huaxue Yu Shengwu Wuli Xuebao DATE: 1992 VOLUME: 24 NUMBER: 1 PAGES: 61-5 CODEN: SHWPAU ISSN: 0582-9879 LANGUAGE: Chinese

14/3,AB/54 (Item 13 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

115225432 CA: 115(21)225432k PATENT
Pre S polypeptide of hepatitis B virus, its recombinant manufacture with Escherichia coli
INVENTOR(AUTHOR): Eimi, Yoichi; Teranishi, Yutaka
LOCATION: Japan,
ASSIGNEE: Mitsubishi Kasei Corp.
PATENT: Japan Kokai Tokkyo Koho ; JP 91108494 A2 ; JP 03108494 DATE: 910508
APPLICATION: JP 89242722 (890919)
PAGES: 16 pp. CODEN: JKXXAF LANGUAGE: Japanese CLASS: C12P-021/02A; C07K-015/04B; C12N-001/21B; C12N-015/51B; C12P-021/02J; C12R-001/19J

14/3,AB/58 (Item 17 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

115069606 CA: 115(7)69606n JOURNAL
Pre-S antigen and HBx antigen
AUTHOR(S): Hayashi, Norio; Katayama, Kazuhiro; Kamada, Takenobu
LOCATION: Med. Sch., Osaka Univ., Osaka, Japan,
JOURNAL: Rinsho Kensa DATE: 1991 VOLUME: 35 NUMBER: 1 PAGES: 54-6
CODEN: RNKNAT ISSN: 0485-1420 LANGUAGE: Japanese

14/3,AB/60 (Item 19 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

114141089 CA: 114(15)141089v JOURNAL
Peptide mapping of neutralizing and nonneutralizing epitopes of duck hepatitis B virus pre-S polypeptide
AUTHOR(S): Yuasa, Satoshi; Cheung, Ramsey C.; Pham Quynh; Robinson, William S.; Marion, Patricia L.
LOCATION: Sch. Med., Stanford Univ., Stanford, CA, 94305-5701, USA
JOURNAL: Virology DATE: 1991 VOLUME: 181 NUMBER: 1 PAGES: 14-21
CODEN: VIRLAX ISSN: 0042-6822 LANGUAGE: English

14/3,AB/67 (Item 26 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

111151624 CA: 111(17)151624t DISSERTATION
The pre-S surface proteins of hepatitis B virus: identification, characterization, and membrane insertion
AUTHOR(S): Wong, David T.
LOCATION: Yeshiva Univ., New York, NY, USA
DATE: 1988 PAGES: 188 pp. CODEN: DABBBA LANGUAGE: English CITATION: Diss. Abstr. Int. B 1989, 49(12, Pt. 1), 5496-7 AVAIL: Univ. Microfilms Int., Order No. DA8826937

14/3,AB/68 (Item 27 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

110034817 CA: 110(5)34817b PATENT
Expression in yeast of DNA encoding hepatitis B surface antigen-heterologous antigen fusion proteins for use as vaccines
INVENTOR(AUTHOR): Cabezon, Teresa; De Wilde, Michel; Harford, Nigel
LOCATION: Belg.
ASSIGNEE: Smith Kline-Rit S. A.
PATENT: European Pat. Appl. ; EP 278940 A2 DATE: 880817

APPLICATION: EP 88870008 (880125) *US 9325 (870130)
PAGES: 101 pp. CODEN: EPXXDW LANGUAGE: English CLASS: C12N-015/00A; A61K-039/29B; A61K-039/21B; A61K-039/295B; A61K-039/015B
DESIGNATED COUNTRIES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE

14/3,AB/69 (Item 28 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

108217271 CA: 108(25)217271x PATENT
Hepatitis B virus surface antigen Pre-S HBsAg and its manufacture with genetically engineered Saccharomyces
INVENTOR(AUTHOR): Mukai, Hiromichi; Tsujikawa, Muneo; Horii, Hajime; Kawabe, Haruhide; Arimura, Hirobumi; Nishida, Masayuki; Suyama, Tadakazu
LOCATION: Japan,
ASSIGNEE: Green Cross Corp.
PATENT: Japan Kokai Tokkyo Koho ; JP 87236496 A2 ; JP 62236496 DATE: 871016
APPLICATION: JP 8678315 (860407)
PAGES: 14 pp. CODEN: JKXXAF LANGUAGE: Japanese CLASS: C12P-021/02A; C12N-001/16B; C12N-015/00B; C07H-021/04; C12P-021/02J; C12R-001/865J

14/3,AB/77 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00159086
Pre-S gene-coded hepatitis B peptides and immunogens and vaccines comprising them
Pre-S genkodierte Hepatitis B Peptide und diese enthaltende Immunogene und Vakzine
Peptides codes par le gene pre-S de l'hepatite B et immunogenes et vaccines les contenant
PATENT ASSIGNEE:
New York Blood Center, Inc., (228440), 310 East 67 Street, New York, New York 10021, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;NL;SE)
CALIFORNIA INSTITUTE OF TECHNOLOGY, (294950), 1201 East California Boulevard, Pasadena California 91125, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;NL;SE)
INVENTOR:
Neurath, Alexander Robert, 230 East 79 Street, New York New York 10021, (US)
Kent, Stephen B. H., 615 West California Boulevard, Pasadena California 91105, (US)
LEGAL REPRESENTATIVE:
Percy, Richard Keith et al (46441), Patents Department British Technology Group Ltd 10 Fleet Place, London EC4M 7SB, (GB)
PATENT (CC, No, Kind, Date): EP 154902 A2 850918 (Basic)
EP 154902 A3 871216
EP 154902 B1 950524
APPLICATION (CC, No, Date): EP 85102250 850228;
PRIORITY (CC, No, Date): US 587090 840307; US 698499 850205
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: C07K-007/04

ABSTRACT EP 154902 A2
Pre-S gene coded peptide hepatitis B immunogens, vaccines, diagnostics, and synthetic lipid vesicle carriers.
A hepatitis B vaccine containing a peptide with an amino acid chain of at least six consecutive amino acids within the pre-S gene coded region of the envelope of hepatitis B virus. The vaccine being free of an amino acid sequence corresponding to the naturally occuring evelope proteins of hepatitis B virus and a physiologically acceptable diluent. The peptide

being free or linked to a carrier. The carrier being a conventional carrier or a novel carrier including a lipid vesicle stabilized by cross-linking and having covalently bonded active sites on the outer surface thereon. Such novel carrier being useful not only to link the novel peptide containing an amino acid chain with amino acids within the pre-S gene coded region of the surface antigen of hepatitis B virus, but can also be used to bind synthetic peptide analogues of other viral proteins, as well as bacterial, allergen and parasitic proteins of man and animals. The peptides of the invention can be utilized in diagnostics for the detection of antigens and antibodies.
ABSTRACT WORD COUNT: 187

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9927	966
CLAIMS B	(German)	9927	984
CLAIMS B	(French)	9927	1067
SPEC B	(English)	9927	15615
Total word count - document A			0
Total word count - document B			18632
Total word count - documents A + B			18632

14/3,AB/81 (Item 3 from file: 654)
DIALOG(R)File 654:US PAT.FULL.

3375132
Derwent Accession: 1985-237979
Utility
C/ **Pre-S gene coded peptide hepatitis B immunogens, vaccines, diagnostics, and synthetic lipid vesicle carriers**
Inventor: Neurath, Alexander R., New York, NY
Kent, Stephen B. H., Pasadena, CA
Assignee: New York Blood Center, Inc. (02), New York, NY
California Institute of Technology (02), Pasadena, CA
California Institute of Technology
New York Blood Center Inc (Code: 13190 59413)
Examiner: Brown, Johnnie R. (Art Unit: 183)
Assistant Examiner: Mohamed, Abdel A.
Law Firm: Sprung Horn Kramer & Wood

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 5204096	A	19930420	US 89338028	19890414
Division	US 4847080	A		US 85698499	19850205
CIP	Abandoned			US 84587090	19840307
Priority				US 89338028	19890414
				US 85698499	19850205
				US 84587090	19840307

Abstract:
A hepatitis B vaccine containing a peptide with an amino acid chain of at least six consecutive amino acids within the pre-S gene coded region of the envelope of hepatitis B virus. The vaccine being free of an amino acid sequence corresponding to the naturally occurring envelope proteins of hepatitis B virus and a physiologically acceptable diluent. The peptide being free or linked to a carrier. The carrier being a conventional carrier or a novel carrier including a lipid vesicle stabilized by cross-linking and having covalently bonded active sites on the outer surface thereon. Such novel carrier being useful not only to link the novel peptide containing an amino acid chain with amino acids within the pre-S gene coded region of the surface antigen or hepatitis B

virus, but can also be used to bind synthetic peptide analogues of other viral proteins, as well as bacterial, allergen and parasitic proteins of man and animals. The peptides of the invention can be utilized in diagnostics for the detection of antigens and antibodies.

Document type: C

?